



THYROID CANCER

Specific RET mutations and cancer outcomes in MEN2A medullary thyroid cancer

BACKGROUND

Medullary thyroid cancer is a rare cancer and comprises 1-2% of the thyroid cancers in the US. Importantly, medullary thyroid cancer has a clear genetic component with RET oncogene and mutations in the RET gene cause this cancer. Medullary thyroid cancer can occur by itself (sporadic) or can run in families by itself or as part of a genetic syndrome. One important genetic syndrome is Multiple Endocrine Neoplasia type 2A, which includes medullary thyroid cancer, an adrenal tumor known as a pheochromocytoma, and parathyroid adenomas that lead to hyperparathyroidism. Almost all patients with MEN2A develop medullary thyroid cancer at some point in their life.

We have come to understand not all RET mutations are the same - that only some mutations correspond to risk of early development of medullary thyroid cancer and that others correlate with more aggressive medullary thyroid cancer. The 2015 American Thyroid Association guidelines for management of medullary thyroid cancer categorize MEN2A mutations into 3 categories – low, moderate, and high risk. This study examined the association of these mutations with the aggressiveness of the cancer.

THE FULL ARTICLE TITLE

Voss RK et al Medullary thyroid carcinoma in MEN2A: ATA moderate- or high-risk RET mutations do not predict disease aggressiveness. *J Clin Endocrinol Metab* 2017;102:2807-13.

SUMMARY OF THE STUDY

At MD Anderson, 262 MEN2A patients with a moderate or high-risk medullary thyroid cancer mutation and

medullary thyroid cancer were examined. They looked at overall survival and time to development of spread of the medullary thyroid cancer outside of the neck between patients with a moderate-risk RET mutation (127 patients) and a high-risk RET mutation (135 mutation). There was no difference in percentage of patients that developed spread of the medullary thyroid cancer outside of the neck or the time to development of spread of the medullary thyroid cancer outside of the neck between the groups. Overall survival was also not statistically significant between the two groups. Medullary thyroid cancer did develop at a younger age in patients with high-risk RET mutations.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The current study challenges the implications of being diagnosed with a high- vs moderate-risk MEN2A RET mutation. The high-risk mutation group did develop medullary thyroid cancer at a significantly younger age, which would confirm the ATA recommendation to perform surgery to remove the thyroid (thyroidectomy) at a younger age in these patients. However, the moderate- and high-risk group had similar outcomes, and therefore, renaming the groups “early” and “late” onset (rather than ‘risk’) may be more appropriate.

— Melanie Goldfarb MD, MSc, FACS, FACE

ATA THYROID BROCHURE LINKS*

Thyroid Cancer (Medullary): - <https://www.thyroid.org/medullary-thyroid-cancer/>

Thyroid Surgery: <https://www.thyroid.org/thyroid-surgery/>

ABBREVIATIONS & DEFINITIONS

Medullary thyroid cancer: a relatively rare type of thyroid cancer that often runs in families. Medullary

cancer arises from the C-cells in the thyroid and is associated with mutations in the RET oncogene





THYROID CANCER, continued

MEN2A: Multiple endocrine neoplasia, type 2A. A hereditary syndrome in which medullary thyroid cancer is often seen in association with other endocrine tumors such as pheochromocytoma (a tumor of the adrenal glands) and hyperparathyroidism (elevated parathyroid hormone levels usually caused by tumors of the parathyroid glands).

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

Mutation: A permanent change in one of the genes.

